# Normal Bladder

## Introduction

The Bladder series covers the structure, function, and failure of everything urine from the renal pelvis to the urethral meatus. The next lesson will cover micturition physiology, sphincters, and autonomics. The final lesson closes with issues unique to males, given their prostate.

This lesson covers bladder anatomy and bladder and urethra embryogenesis, then focuses on the urethra, with highlights on pathologic states of the urethra and ureters as they relate to the bladder. But first we start where we left off with the Kidney series, at the ureteropelvic junction. The glomeruli have filtered fluid and small molecules. The tubules selectively resorbed water and small molecules and also secreted some others. What comes out of the nephrons is a dilute urine that passes through the collecting ducts on its way to the minor calyces. The collecting duct can choose to resorb the miniscule amount of remaining sodium (aldosterone) or water (ADH). Regardless, the collecting ducts drain into the calyces. Urine is made. From this point forward anatomically, urine is not modified. Urine is drained down the ureters into the bladder, where it is stored. The bladder fills. Then, when the person is ready to void, the bladder empties through the urethra.

## Ureters

The ureters exit the kidney at the ureteropelvic junction. There they descend to the bladder. The ureters pass over the common iliac artery at the pelvic brim, then under the uterine artery (women) or the vas deferens (men), then connect with the corners of the trigone. The ureters penetrate obliquely to the detrusor muscle, and arise at the base of the trigone of the bladder, centimeters from the opening of the urethra. The **ureteropelvic** junction is between the ureter (uretero-) and the pelvis of the kidney (-pelvic). The **ureterovesical** junction is between the ureter (uretero-) and the bladder (-vesiculo).

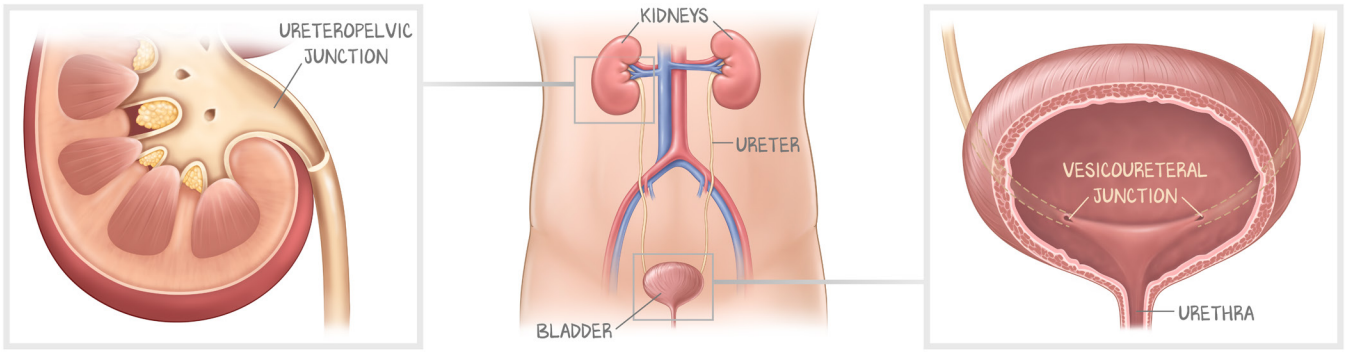


**Figure 1.1: Ureter Anatomy**
The ureteropelvic junction is where the ureters begin, confluent with the renal pelvis. The ureters descend the retroperitoneum and into the pelvis, where they insert into the underside of the bladder. The ureterovesical junction is where the ureters enter the bladder to form the base of the trigone.

The ureters are retroperitoneal for their entire course. There are three points of slight narrowing that predispose the ureters to obstruction, especially by stones. The **ureteropelvic junction** is the most common site of obstruction. Where the ureters pass over the external or common iliacs is another common site. Finally, the **ureterovesical junction**. The endpoints, where the ureters are interacting with another organ, are easy to understand and remember. Therefore, it is often the common iliacs that make their ways onto board exams.

The ureters are lined with **transitional cell epithelium**, which sits above a submucosal layer of connective tissue. Surrounding that is an outer and inner **smooth muscle layer**. This smooth muscle layer is responsible for **peristalsis** and the propelling of urine unidirectionally to the bladder. The ureters act as conduits for urine from the kidney to the bladder. Blockade of ureteral outflow to the bladder will result in the accumulation of fluid and generation of backpressure toward the kidney. This causes **hydroureter—**dilated ureters and a sign of obstruction (as discussed in Injury #1: *Renal Pathology – Kidney Injury I Approach*).

The reason why the ureters penetrate the bladder through the detrusor muscle at an oblique angle is to ensure unidirectional flow of urine out of the bladder through the urethra. When a person voids urine, it is under high pressure. What took hours for the kidneys to make and for the bladder to store is released into the toilet in a matter of seconds. That means the detrusor muscle contractions are strong. The urine will flow through the path of least resistance. That is supposed to be the urethra (which opens) and not the ureters (which should close). But the ureters are just hollow tubes. The way the ureters close is by contraction of the detrusor. By entering at an oblique angle, when the detrusor squeezes, it squeezes shut the ureter.

An incompetent vesicoureteral orifice allows the reflux of bladder urine into the ureters (**vesicoureteral reflux**). Often caused by a **missing intravesicular component** of the ureter (not enough ureter is through the detrusor to get clamped down on), this disease presents as a **congenital defect**, present from birth, where a child will suffer repeated urinary tract infections or pyelonephritis. Up to 10% of live births have vesicoureteral reflux. Most are asymptomatic and don't get infections. Most will be corrected spontaneously as the child grows. There is still back pressure to the kidney, which can result in cortical scarring later in life, but the vast majority of patients have no perceivable increased risk of chronic kidney disease. The way this will present on an exam is as a severe case in which the patient presents with **pyelonephritis and hydronephrosis**.

For the test, the congenital defect that causes hydronephrosis and UTIs in boys is posterior urethral valves (see below). The congenital defect that causes hydronephrosis and pyelonephritis in girls is vesicoureteral reflux.

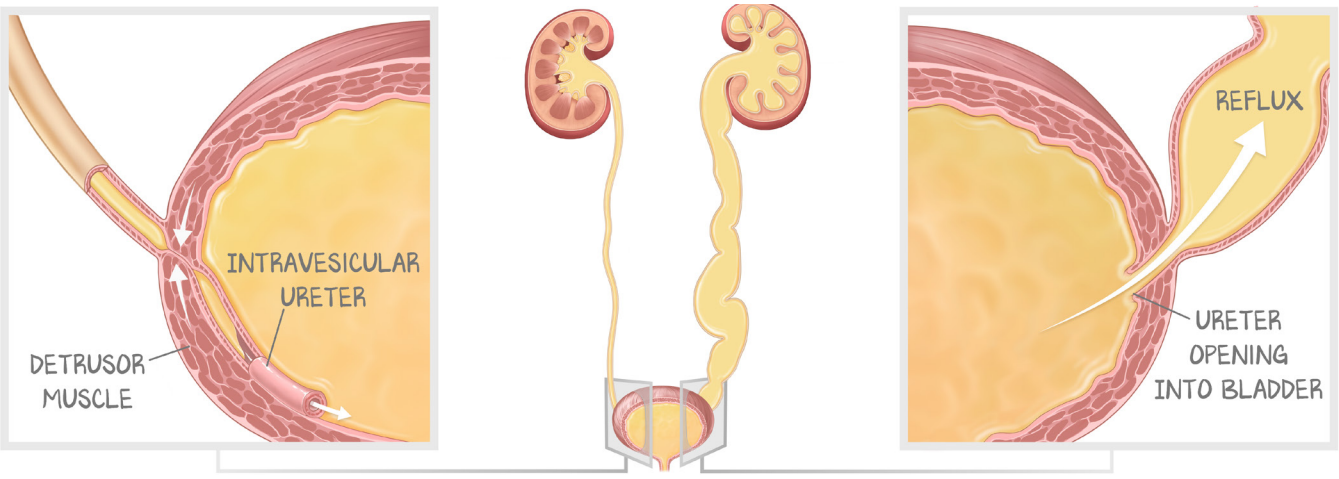


**Figure 1.2: Vesicoureteral Reflux**
A voiding cystourethrogram demonstrates reflux into the ureters and kidney. No contrast should be visible in the ureters. On the left side of the illustration, a normal-length ureter passes well into the bladder, such that a contraction of the detrusor muscle will clamp the ureter before urine can reflux up the long tube. On the right side of the illustration, an exaggerated loss of ureter length into the bladder causes urine to reflux up into the ureter. Once there is a flow of refluxed urine, the urine continues to flow until the bladder is emptied.

## Bladder Anatomy

The ureters form from the renal pelvis, travel along the **anterior surface of the psoas muscles**, and move from their **retroperitoneal origin** into the **peritoneal cavity** as they **cross the external iliac arteries** as they pass over the pelvic brim. There, the ureters, one on each side, make contact with the bladder. These contact points are quite low, and posterior on the bladder.

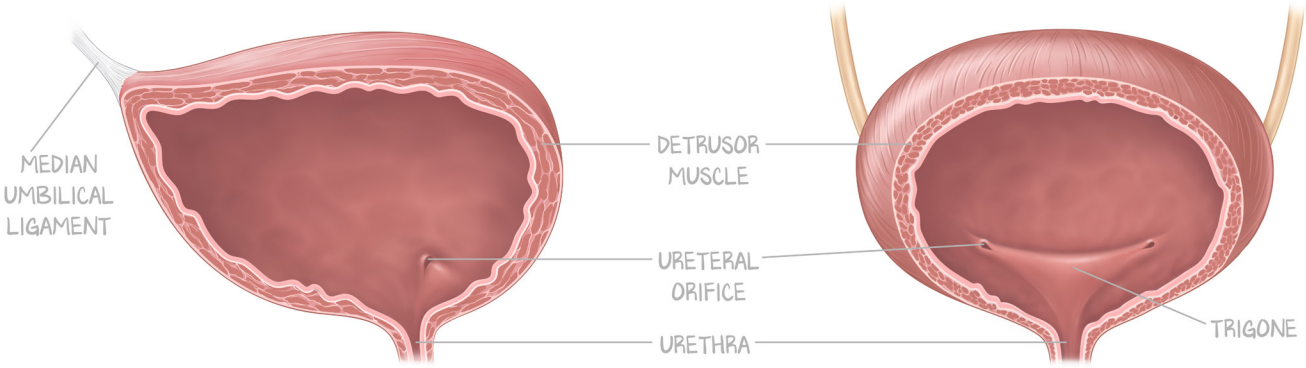


**Figure 1.3: Bladder Anatomy**
A sagittal section shows the orientation of the median umbilical ligament (embryonically the allantois) at the dome of the bladder and the relative proximity of the ureteral orifice and the urethra. A coronal illustration shows the orientation of the ureters on the back and base of the bladder, again near the urethra. The triangle of smooth tissue formed by the connection of the urethra and the ureters is the trigone.

The bladder itself is a hollow organ, designed to hold the urinary volume. It is lined with **transitional cell epithelium** and is surrounded by the **detrusor muscle**. The detrusor muscle is all around the bladder and can contract and relax like a sphere.

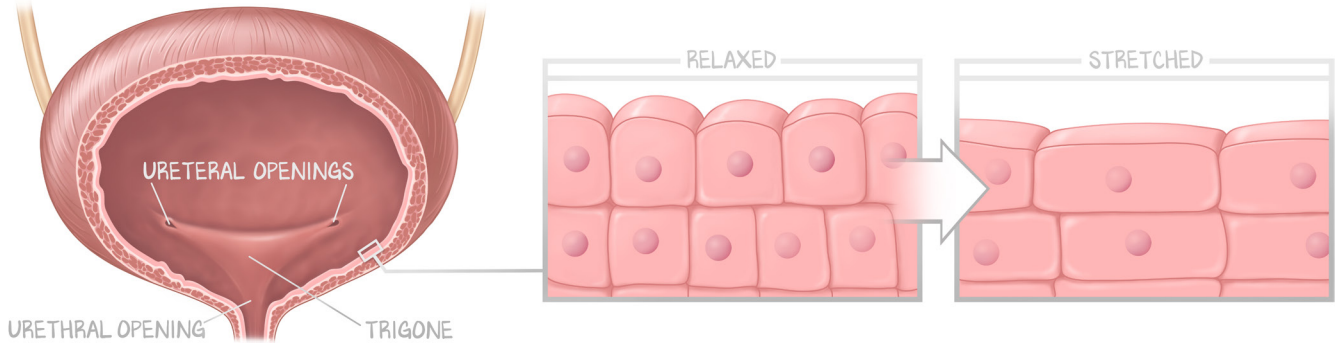


**Figure 1.4: Bladder Histology**
Transitional cell epithelium is capable of changing from a columnar (relaxed) epithelium to a squamous (stretched) epithelium. Transitional cell epithelium predominates in the urinary system, from the calyces and pelvis, down the ureter, into the bladder, and the beginning of the urethra. Only the trigone of the bladder is not transitional cell epithelium.

The **trigone** is a triangular-shaped structure of **smooth tissue** unlike the rest of the bladder wall. It is a triangle along the floor of the bladder. The apex of the triangle is **continuous with the opening to the urethra** and is the exit of the bladder. The base of the trigone is made by the ureteral openings and is the entrance of the bladder. Both **ureters** connect **under** the bladder. The two inputs to the bladder penetrate the bladder very close to the exit. The bladder will fill with urine until the urethra is opened, when urine will drain.

The urethra has two sphincters. A complex arrangement of somatic and autonomic innervation regulate the bladder and urethra. We are saving the details of that for the next lesson (Bladder #2: *Micturition*). We're going to pass right over those details in this lesson, focusing on the urethra's segments and not the smooth muscle around it.

## Urethra

The exit of the bladder is the opening of the urethra. Like the ureters, the urethra is a tube that carries urine. Unlike the ureters, there is no peristalsis in the urethra. Therefore, the urethra is simply a tube that carries urine from the bladder to outside the body. The complexity of the urethra comes in two forms—the urethral sphincters that regulate continence, and the change in epithelium.

The urethra looks different in males and females—the male urethra runs through an additional appendage, so must be longer. The urethra in males can be divided into different segments relative to where it is along the prostate or penis. In females, we don't have to worry about such considerations. What is shared between males and females is that the urethra is divided into a posterior and anterior segment. The **posterior urethra** (proximal urethra, vesicular urethra) is lined by **transitional cell epithelium**, similar to the bladder it originates from. The **anterior urethra** (distal urethra) is lined by **stratified squamous epithelium**, similar to the skin which the exit of the urethra is continuous with. For females, there is only that—posterior/transitional then anterior/stratified squamous. For males, a bit more of a discussion is needed. The posterior urethra is the same in males as in females, running from the bladder to the exit through the pelvic floor muscles. Same length, same function. The anterior urethra is much different, accounting for the significantly longer urethra in males.

In males, the **posterior urethra** can be subdivided by the relationship with the prostate gland—prostatic or membranous. From the bladder through the length of the prostate is the **prostatic** urethra. The itty bitty stretch of posterior urethra from the end of the prostate to the pelvic floor, where the external urethral sphincter is located, is **membranous** urethra. When out from underneath the pelvic floor muscles the urethra transitions to the **anterior urethra**. The entirety of the male anterior urethra is sometimes called spongy urethra, and sometimes segmented rather ambiguously into the bulbous, penile, then ultimately glandular urethra. But here's the thing—there isn't any real difference in function, physiology, disease, or pharmacology between the female anterior urethra and the male anterior urethra except for the length (males 16 cm, females 1 cm). In both sexes, there is a gradual change from transitional cell epithelium at the bladder to stratified squamous cell epithelium at the urethral opening. In males, that transition is drawn out over the length of the anterior urethra. In males, there is a change from obviously transitional cell in the posterior urethra to pseudostratified columnar or stratified columnar epithelium along the middle segments, then eventually into the stratified squamous epithelium. Female anterior urethras have been shown to demonstrate similar epithelia. It's just that because they are so short, that transition through columnar happens quickly.

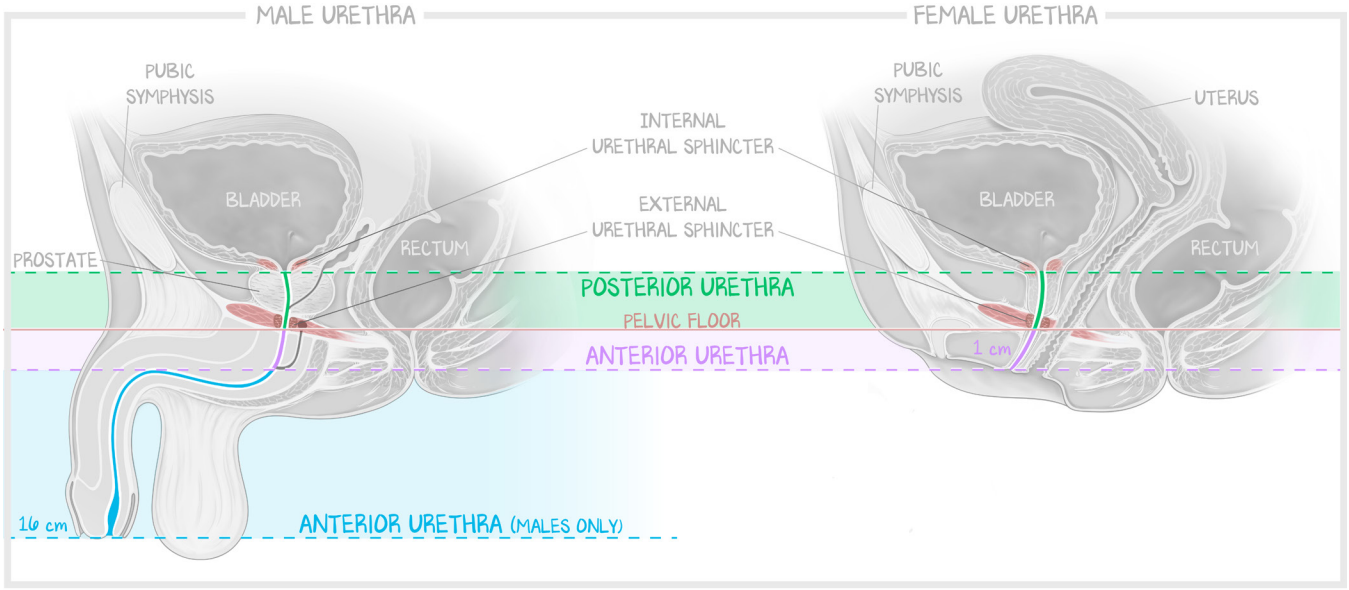


**Figure 1.5: Urethra**
The posterior urethra is the same in males and females, running from the bladder, where the urethra begins, to the pelvic floor, where the posterior urethra ends. Notice that also means the posterior urethra is regulated by both the external and internal urethral sphincters. The anterior urethra is very short in females, but much longer in males, given the additional appendage of the penis.

## Urethral Pathology

**Posterior urethral trauma** will be damage at or above the pelvic floor. This type of urethral injury typically occurs from **pelvic fractures**. To fracture the pelvis takes enormous force, so will be an unrestrained motor vehicle collision with obvious hip rocking on physical exam. There will be **gross hematuria**. Because the posterior urethra is so visceral, having damage to the posterior urethra could indicate damage to the bladder as well. A **perforated bladder** could be either retroperitoneal or intraperitoneal.

**Anterior urethral trauma** will be damage of the anterior urethra—anywhere within the penis in males and a very short segment distal to pelvic floor muscles in females. Because the anterior urethra is so much longer in males, trauma is more often seen in males. This is seen in **saddle injuries** where the urethra is crushed between the pubic bone (which does not fracture) and a cylindrical fixed object, such as a horizontal pole or bicycle frame. Visualize either a female falling straight down onto a horizontal pole or a male falling on a pole while erect (so the penis is not injured). Remember that the urethral opening is pointed DOWN when the patient is standing up, not FORWARD as when seated on a toilet.

**Posterior urethral valves** are not valves at all, nor are they posterior in relation to something. The diagnosis "posterior urethral valves" (PUV) is an embryologic defect of the **posterior urethra** that obstructs outflow of urine from the developing bladder. The tube, which should be hollow, has a **membrane** (a general term that means "tissue dat don't belong") covering it. This **occurs only in males**. This leads us at OME to believe that it has nothing to do with the membranous urethra, as is proposed, because that is the segment present in females as well. The extension of the urethra into the bulbous penis requires more urethra, more tissue to be generated. That generating of extra tissue sets up the possibility that extra tissue could end up blocking the lumen of the bulbous anterior urethra. It has gotten the name "valve" because the membrane does not prevent a medical professional from inserting an indwelling catheter (allows movement one way) but does prevent the baby from peeing (restricts movement the other way). Really, it is just extra tissue in the way. Sometimes, simply placing the catheter tears the membrane and fixes the problem. Other times, cystoscopy is required to clip away

the excess tissue and alleviate the condition. The name remains, **posterior urethral valves** (PUV), so that's what we're teaching. The degree to which the lumen is blocked determines the severity of the disease. This is an outflow obstruction. Urine cannot get out of the bladder, so backs up. The bladder distends. The pressure is translated to the developing kidneys. At its most severe, the kidneys will fail, or fail to form, resulting in the absence of kidneys. This would present like Potter's sequence with oligohydramnios and an abysmal prognosis. At its least severe, there is normal gestation and delivery, and the patient will receive an ultrasound for a urinary tract infection (boys shouldn't get UTIs); the ultrasound will reveal **hydronephrosis**. Because the obstruction is at the level of the urethra, there will be **bilateral hydronephrosis**. That hydronephrosis can be detected in utero. The congenital defect that causes hydronephrosis and UTIs in boys is posterior urethral valves. The congenital defect that causes hydronephrosis and pyelonephritis in girls is vesicoureteral reflux.

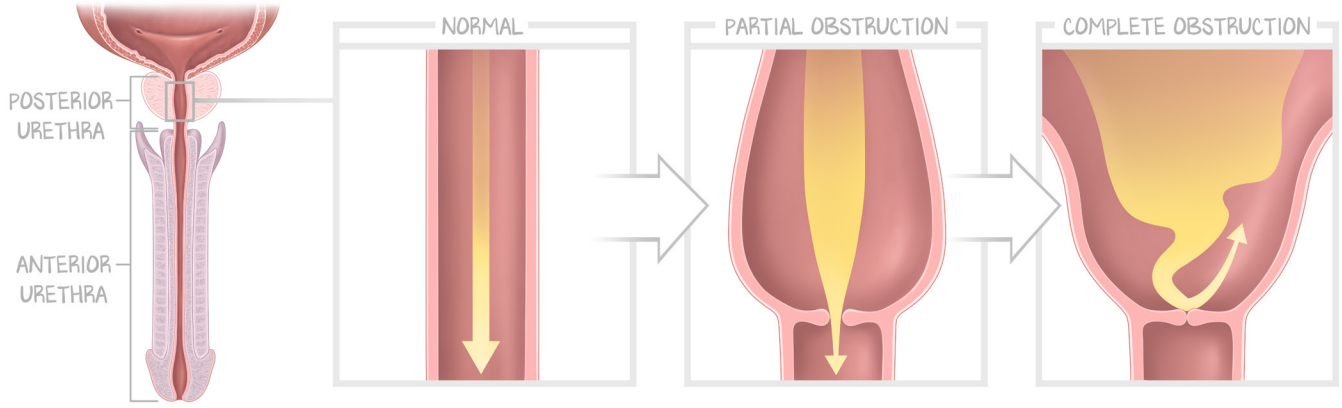


**Figure 1.6: Posterior Urethral Valves**
In normal male development, the anterior urethra must be elongated and does not result in an obstructive membrane, hydroureters, hydronephrosis, or renal impairment. If a membrane forms and only partially obstructs the urethra, bilateral hydroureter develops as back pressures are translated from the bladder to both ureters. In near-total occlusion, there is massive hydronephrosis and consequent renal failure. A complete membrane would result in oligohydramnios and renal failure at birth.

## Embryology of Bladder and Urethra

The cloaca is the end of the gut tube, made from endoderm. The cloaca is divided into the rectum and the urogenital sinus by the urogenital fold. The urogenital sinus will become the bladder and urethra. The bladder and urethra come from the gut tube, and so are from **endoderm**. They will be lined by transitional cell epithelium. It is important to note that the ureters, derived from **mesoderm**, which originate as the ureteric bud from the mesonephric duct, will also be lined by the same transitional cell epithelium.

We want to pay attention to the **urogenital sinus**. It is divided into 3 parts—cranial, middle, and caudal.

The most cranial structure is the largest structure. It will **become the bladder**. This pre-bladder structure is a reservoir for fluid waste. Before the kidneys, urethra, and bladder are well formed, liquid waste is managed by the umbilical cord. The connection between the bladder and the umbilical cord is via the **allantois**. While the allantois is the "urine-out tube" of the urogenital sinus, the allantois does NOT become the "urine-out tube" of the bladder—the allantois does not become the urethra. The urethra is derived from the urogenital sinus. The allantois becomes the fibrous urachus, and should fuse to form the **median umbilical ligament**. A failure of the allantois-turned-urachus to fuse results in a **patent urachus**, which presents as urine draining for the umbilicus (there other variations of this, but the disease state you should commit to memory is patent urachus draining fluid through the umbilicus at birth).

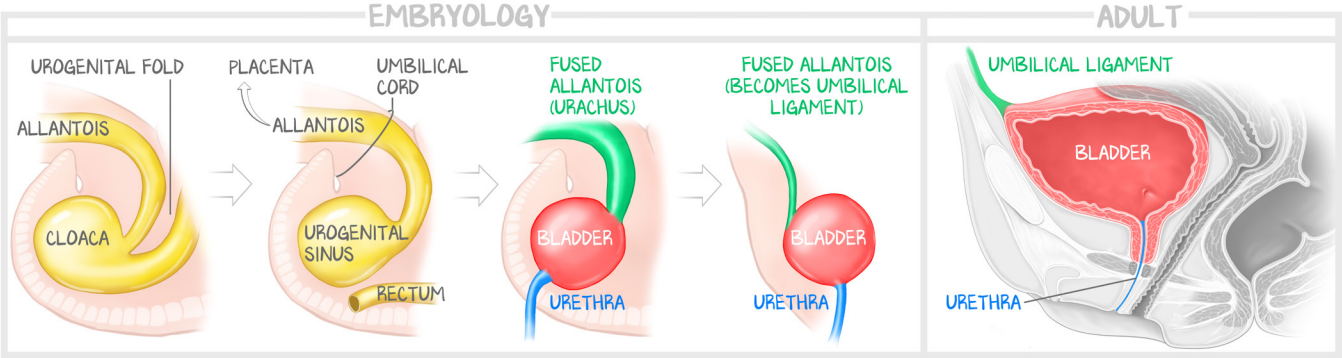


**Figure 1.7: Bladder Embryology**

The middle part of the urogenital sinus will form the **urethra**. Females, who exhibit the default human genetic pattern, have a short urethra, and so require no additional growth. In males, who exhibit additional gene expression by the presence of testosterone from the Y chromosome, the urethra must be extended to accommodate the growth of the male appendage—the penis. This extra tissue, both endodermal urethra and ectodermal skin, is why males alone can have the congenital defect named posterior urethral valves.

The caudal part of the urogenital sinus will become the lower vagina and clitoris. The vagina can be induced to scrotum, the clitoris induced to a penis. More on that in the Reproduction module. Hypospadias and epispadias are also discussed in the Reproduction module.

## Bladder Cancer

There is little to know about bladder cancer. Not that it isn't important, only that it doesn't have much to do with Basic Sciences. Much is based on the diagnostic pathway, intravesicular chemo, resection or not, etc. Those are management decisions. Basic Sciences remains focused on mechanisms.

What you should know is that bladder cancer is usually a malignancy of **transitional cell epithelia** and is associated with **aniline dyes** and **aromatic amines** (dry cleaning industry), **cyclophosphamide** (hemorrhagic cystitis is a complication of cyclophosphamide and the risk factor for malignancy), and **cigarette smoking**. The presentation is usually **painless hematuria** and sometimes obstruction. You may have heard the phrase, "*transitional cell carcinoma is the most common malignancy of the urinary tract.*" Since the epithelium of the ureters, bladder, and urethra until the very end, are all lined by transitional cell epithelium, it is the only malignancy of the urinary tract possible!

Except . . . there are always excepts. **Schistosomiasis** (Microbiology, Parasites #2: *Helminths*), specifically *S. haematobium,* can cause **squamous cell carcinoma** of the bladder. Laying its eggs in the venous plexus of the bladder, the eggs must pass through the epithelium to be released in the urine. This causes inflammation. Inflammation induces metaplastic changes before progressing to dysplasia. On your test, look for a young Middle Eastern man with bladder cancer. The young age implies a different pathogenesis thank transitional cell, and the geographic location indicative of schistosomiasis risk.

While squamous cell carcinoma of the bladder is possible, you should learn that bladder cancer is urothelial carcinoma is transitional cell carcinoma. It happens in old people who smoked.